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First Named Inventor:	WIGHTMAN, PAUL D.		
Application No.:	10/821335	Confirmation No.:	9992
Filed:	April 9, 2004	Group Art Unit	1625
Title:	DELIVERY OF IMMUNE RESPONSE MODIFIER COMPOUNDS		

BRIEF ON APPEAL

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July 27, 2009 /Joyce M. Courtney/

Date Signed by: Joyce M. Courtney

Dear Sir:

This is an appeal from the Office Action mailed on January 27, 2009, finally rejecting claims 1, 3, 11, 12, and 14.

Fees

☒ Any required fee under 37 CFR § 41.20(b)(2) will be made at the time of submission via EFS-Web. In the event fees are not or cannot be paid at the time of EFS-Web submission, please charge any fees under 37 CFR § 1.17 which may be required to Deposit Account No. 13-3723.

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A Notice of Appeal in this application was mailed on May 27, 2009, and was received in the USPTO on May 27, 2009.

Appellants request the opportunity for a personal appearance before the Board of Appeals to argue the issues of this appeal. The fee for the personal appearance will be timely paid upon receipt of the Examiner's Answer.

REAL PARTY IN INTEREST

The real party in interest is 3M Company (formerly known as Minnesota Mining and Manufacturing Company) of St. Paul, Minnesota and its affiliate 3M Innovative Properties Company of St. Paul, Minnesota.

RELATED APPEALS AND INTERFERENCES

Appellants are unaware of any related appeals or interferences.

STATUS OF CLAIMS

Claims 1, 3, 11, 12, and 14 are pending. Claims 10 and 15-51 are withdrawn. Claims 1, 3, 11, 12, and 14 stand rejected.

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STATUS OF AMENDMENTS

No amendments have been filed after the final rejection.

SUMMARY OF CLAIMED SUBJECT MATTER

Independent claim 1 is directed to an IRM-support complex comprising one of a particular group of immune response modifiers (IRMs) covalently bound to a macromolecular support material. The IRM compound is an agonist of Toll-like Receptor (TLR) 6, TLR 7 and/or TLR 8 (page 12, line 150). The IRM must be further selected from the group consisting of imidazoquinoline amines (page 14, lines 12-13); tetrahydroimidazoquinoline amines (page 14, line 20); imidazopyridine amines(page 14, lines 27-28); 1,2-bridged imidazoquinoline amines (page 14, lines 33); 6,7-fused cycloalkylimidazopyridine amines (page 15, line 1); imidazonaphthyridine amines (page 15, line 1); tetrahydroimidazonaphthyridine amines (page 15, line 2); oxazoloquinoline amines(page 15, line 2); thiazoloquinoline amines(page 15, line 2-3); oxazolopyridine amines(page 15, line 3); thiazolopyridine amines (page 15, line 3);

oxazolonaphthyridine amines (page 15, line 3-4); thiazolonaphthyridine amines (page 15, line 4); 1*H*-imidazo dimers fused to pyridine amines; quinoline amines (page 15, line 4-5), tetrahydroquinoline amines(page 15, line 5); naphthyridine amines (page 15, line 5); and tetrahydronaphthyridine amines (page 15, line 6). The IRM may be covalently attached such that it is active while attached to the support material (page 8, line 32- page 9, line 2; page 21, lines 9-14). As a result of this attachment, the IRM has an altered cytokine induction profile *in vivo* (page 2, lines 17-21). Additionally, covalent attachment may reduce systemic absorption of the IRM (page 4, lines 30-34), preventing systemic dosages that often produce adverse or even toxic side effects for the subject (page 25, line 1-2).

Dependent claim 3 further defines the macromolecular support material (page 7, line 29-31) of the IRM-support complex as a material selected from the group consisting of a gel, a foam, a sponge, a fiber, a hydrogel, and a bead (page 19, lines 5-10). Dependent claim 11 defines the macromolecular support material of the IRM-support complex as a material with an average largest dimension of at least 1 nm (page 8, line 7).

Independent claim 12 is directed to an IRM-support complex comprising an immune response modifiers (IRMs) covalently bound to a polymer (page 19, line 11). The IRM is attached in such a way that it is active while attached to the support material (page 21, lines 9-14). Dependent claim 14 further limits the polymer of claim 12 to a bioadhesive polymer (page 20, line 9).

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

I. First Ground of Rejection - § 112 First Paragraph

Claims 1 and 3 stand rejected under 35 USC § 112, first paragraph, as failing to enable one skilled in the art to make all of the claimed IRM-support complexes.

II. Second Ground of Rejection - § 102

Claims 1, 3, 11, 12, and 14 appear to have been rejected under 35 USC § 102 as anticipated by U.S. Patents Nos. 7,030,129 (Miller), 4,689,338 (Gerster); 6,894,060 (Slade), or Langer et al. (1990) New Methods of Drug Discovery. *Science* 249:1527.

III. Third Ground of Rejection - § 103

Claims 1, 3, 11, 12, and 14 stand rejected under 35 USC § 103 as obvious in view of U.S. Patents Nos. 7,030,129 (Miller), 4,689,338 (Gerster); 6,894,060 (Slade) and in further view of Langer et al. (1990) New Methods of Drug Discovery. *Science* 249:1527.

IV. Fourth Ground of Rejection - Nonstatutory Obviousness-Type Double Patenting

Claims 1, 3, 11, 12, and 14 stand rejected on the ground of nonstatutory obviousness type double patenting as purportedly unpatentable over claim 1 of U.S. Patent No. 5,078,978.

ARGUMENT

I. First Ground of Rejection - § 112 First Paragraph

Claims 1 and 3 were rejected under 35 USC § 112, first paragraph, as purportedly failing to comply with the enablement requirement. The issue before the Board is whether the specification would have allowed one skilled in the art to make the claimed IRM-support complexes without undue or unreasonable experimentation.[1] The Applicants' specification enables the formation of IRM-support complexes by covalently attaching different IRMs to a wide range of different supports.

The Examiner stated that "Applicants in their specification have not shown how the bonding takes place on the support."[2] On the contrary, Applicants have provided many different examples of covalently attaching the claimed IRMs to a variety of support materials. Examples 2-6 and 7-11 show covalent linkage to silica; example 13 shows covalent linkage to FEP film, examples 15-16 show covalent linkage to gold; example 21 shows covalent linkage to silica coated superparamagnetic particles; examples 27-29 show covalent linkage to acrylic; examples 30-32 show covalentl linkages to polystyrene. Bonding to each of these types of support is demonstrated in the example, thus clearly enabling the claimed invention.

The Examiner asserts that because the Applicants have exemplified only limited examples, the other IRM-support complexes are not enabled.[3] As the Examiner notes, Applicants have exemplified the linkages of the pyridine imidazole and the quinoline imidazole.[4] While other molecules than those exemplified are included within the claim scope, claim 1 requires that the compounds are from a Markush group of closely related structures and are TLR 6, 7, and/or 8 agonists. These specified molecules have common structural and functional similarities such that one skilled in the art would be able to use the methods of the present disclosure to covalently attach the molecules to a variety of support materials such that the activity of the IRMs is maintained upon attachment. Although some experimentation would likely be required, with the

[1] MPEP §2164.01 ("The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde,* 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable?")
[2] Final Office Action mailed 1/27/09 at 6.
[3] Final Office Action mailed 1/27/09 at 12.
[4] Final Office Action mailed 1/27/09 at 12.

specification's examples as a guide, the experimentation would not be undue.[5] One of ordinary skill in the art would have no difficulty practicing the full scope of the claimed invention.

Applicants submit that the rejection of claims 1 and 3 under 35 USC § 112, first paragraph, should be reversed.

Applicants also wish to note that claim 14 improperly depends from canceled claim 13, but since the limitation of canceled claim 13 was incorporated into claim 12 it is clear that claim 14 should now depend from claim 12. A 112, second paragraph, rejection was not made but this correction will be made before any allowance of the application.

II. Second Ground of Rejection - § 102

Claims 1, 3, 11, 12, and 14 were apparently rejected under 35 USC §§ 102 as anticipated by U.S. Patents Nos. 7,030,129 (Miller), 4,689,338 (Gerster); 6,894,060 (Slade), or Langer et al. (1990) New Methods of Drug Discovery. *Science* 249:1527.

The Applicants respectfully submit that none of the cited references disclose an IRM covalently attached to a support complex, and the final Office Action does not point to any such disclosure. Therefore, Applicants respectfully request the reversal of the rejection under 35 USC § 102.

III. Third Ground of Rejection - § 103

Claims 1, 3, 11, 12, and 14 stand rejected under 35 USC § 103 as obvious over U.S. Patents Nos. 7,030,129 (Miller), 4,689,338 (Gerster); 6,894,060 (Slade) and in further view of Langer et al. (1990) New Methods of Drug Discovery. *Science* 249:1527.

Applicants respectfully submit that none of the cited references, either alone or in combination, fairly discloses the claimed invention or would have motivated one skilled in the art to practice the claimed invention with a reasonable expectation of success. Moreover, none of the cited art would have predicted the surprising result that the claimed IRMs are able to remain active while covalently attached to a macromolecular support complex (claims 1, 3, and

[5] MPEP §2164.01, citing *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976) ("The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue.")

11) or polymer (Claims 12 and 14). This has many potential benefits in terms of controlling delivery and limiting systemic exposure to the IRM compounds.

1. Gerster, Slade, and Miller do not disclose the covalent attachment of IRMs to a macromolecular support material or polymer.

Claims 1, 3, and 11, and 12 and 14 require covalent attachment of an IRM to a macromolecular support material or a polymer, respectively.

The Examiner notes that the specification discusses mixing or blending the IRM compound into a carrier,[6] as suggested by Gerster,[7] Miller,[8] and Slade.[9] In contrast, however, the pending claims are limited to an IRM covalently bonded in an IRM-support complex or polymer. Unlike Gerster, Miller, and Slade, the IRM is not merely mixed into the carrier. A covalent bond would not form if an IRM was simply mixed with the carrier. As shown in the present application, specific and intentional chemical reactions are run in order to make the covalently attachment. Moreover, nothing in Gerster, Miller or Slade suggests that a covalently attached IRM compound will remain active while attached to the support material or polymer.[10]

2. Langer does not disclose the covalent attachment of IRMs to a macromolecular support material or polymer.

Langer discloses that chemical modification of some drugs can be used to alter their biodistribution and does suggest covalently attaching drugs to macromolecules.[11] However, Langer does not teach or suggest attaching the claimed IRM compounds to a macromolecular support or polymer, or that such molecules can remain active while they are attached. While the Examiner suggests Langer provides "considerable motivation to one of skill in the art to make complexes of known drugs,"[12] Langer does not disclose or suggest what types of drugs may be effective when conjugated or how such a complex could be enabled. More specifically, Langer does not disclose or suggest the covalent attachment of the claimed IRM compounds to a

[6] Final Office Action mailed 1/27/09 at 6.
[7] *Id.* (Gerster discloses the administration of IRMs in vehicles such as solutions and creams.)
[8] *Id.* (Miller discloses IRM compounds delivered in a gel, paste, or similar substance.)
[9] *Id.* (Slade discloses the administration of IRMs in creams, gels, lotions, ointments, or sprays.)
[10] Specification, page 8, line 32- page 9, line 2; page 21, lines 9-14.
[11] Final Office Action mailed 1/27/09 at page 7.
[12] Final Office Action mailed 1/27/09 at page 4.

macromolecular support material (claims 1, 3 and 11), nor would there be any reasonable expectation of success based on Langer.

With regard to polymers in particular, Langer teaches the use of degradable polymers to lengthen the lifetime or alter the immunogenicity of a drug. In contrast to the claimed invention where an IRM can remain biologically active while it is covalently bound to a polymer, drugs undergoing controlled release become active upon release. One skilled in the art would not assume from Langer that all drugs can be beneficially attached to a polymer, how such attachment is to be made, or that controlled release from a degradable polymer is necessary or desirable, and, again, nothing in Langer suggests that the claimed IRM compound types could be attached to a polymer and remain active while attached.

3. The combination of Gerster, Slade, and Miller with Langer does not render the covalent attachment of IRMs to a macromolecular support material or polymer obvious.

Gerster, Slade, and Miller teach the therapeutic use of IRMs in a carrier. Langer discloses that forming complexes of some drugs with macromolecules or polymers may improve their delivery.[13] The Examiner combines Langer with Gerster, Slade, and Miller to conclude that "one of skill in the art of drug delivery would have been motivated to make the macromolecular complexes of the IRM compounds to enhance the delivery of the compounds [to] specific sites."[14] However, none of the cited references teach or suggest (i) covalently attaching the IRM compounds of the current invention to a macromolecule or polymer or (ii) the surprising result that the presently claimed IRM compounds can remain functionally active while they are attached to a macromolecule or polymer.

Furthermore, the covalent attachment of an IRM to a macromolecule or polymer is not just the "mere substitution of one element for another."[15] As Langer notes, the process of attachment "alters the drug's size and other properties, resulting in different pharmacokinetics and biodistribution."[16] In fact, Langer discloses the covalent attachment of drugs to macromolecules only via degradable linkages where the drug becomes active upon its release

[13] Final Office Action mailed 1/27/09 at 10.
[14] Final Office Action mailed 1/27/09 at 10.
[15] MPEP § 2141, citing *KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. ___, 82 USPQ2d 1385 (2007).
[16] Langer (1990) at page 1527.

from the macromolecule.[17] Similarly, Langer focuses on attaching drugs polymers to create controlled release systems that store inactive drugs and release active drugs.[18] The techniques disclosed by Langer alter a drug's pharmacokinetics (activity). Similarly, covalently bonding an IRM to a macromolecular support or polymer could have decreased or completely eliminated IRM activity. Thus, not only is there a lack of motivation and reasonable expectation of success, but the surprising result that the claimed IRMs are functionally active while covalently bonded was completely unpredictable. Thus, the combined teachings of Gerster, Slade, Miller and Langer do not render the covalent attachment of IRMs to a macromolecular support material or polymer obvious.

The Applicants respectfully submit that none of the cited references, either alone or in combination, would have motivated one skilled in the art to covalently bond an IRM in an IRM support complex to either a macromolecular support material or a polymer.

Further, with particular regard to claim 11, nothing in the cited references discloses attachment to macromolecular support material having an average largest dimension of at least 1 nm. Therefore, claim 11 is deemed unobvious for this reason as well.

4. The disclosure of avidin-biotin affinity based technology in the specification does not render the covalent attachment of IRMs to a macromolecular support material obvious.

The Examiner states that Applicants' "own priority admits that covalent bond exists between avidin-biotin affinity based technology."[19] While Applicants did state in their specification that IRMs could be non-covalently attached to a macromolecular support material[20] and one example of non-covalent attachment is the avidin-biotin system,[21] the current claim set is limited to covalent linkage of the IRM to the macromolecular support material. The covalent bond in the IRM-support complex is a key aspect of the claimed invention and is not anticipated by avidin-biotin affinity based technology.

5. The covalent attachment of unrelated compounds to support materials does not render the covalent attachment of IRMs to a macromolecular support material obvious.

[17] *Id.*
[18] *Id.* at 1530-31
[19] Final Office Action mailed 1/27/09 at 2.
[20] Specification, page 27, lines 19-22.
[21] Specification, page 27, lines 23-24.

The Examiner states that "it is well known that compounds can be covalently bonded" to solid supports.[22] The Examiner goes on to mention (but not expressly apply as a rejection) U.S. Patents No. 5,078,978 (Tarbet) and WO 2001/023067 (Ronald) which demonstrate the covalent bonding of alkoxysilanes and polyamides to solid supports. While Applicants understand that the covalent bonding of pharmaceutically active compounds may have been done before, it was not routine or conventional, nor was it assumed that the results would be successful or beneficial. Indeed, neither Tarbet or Ronald suggests that an IRM compound can retain its activity while attached. Thus, there would have been no motivation or expectation of success in attaching IRMs to a solid support, or how to covalently attach the claimed IRMs to a solid support, or that one can preserve the activity of the IRM when attached to a solid support.

In conclusion, none of the cited references render the covalent attachment of an IRM to a macromolecular support material or polymer obvious. Therefore, Applicants respectfully request the reversal of the rejection under 35 USC § 103 and the allowance of claims 1, 3, 11, 12, and 14.

IV. Fourth Ground of Rejection - Nonstatutory Obviousness-Type Double Patenting

Claims 1, 3, 11, 12, and 14 were rejected on the ground of nonstatutory obviousness type double patenting as purportedly unpatentable over claim 1 of U.S. Patent No. 5,078,978. U.S.

First, as a formal matter, Patent No. 5,078,978 is not owned by 3M and is not drawn to the same subject material. It is clearly an error and should be reversed.

Second, it appears the Examiner may have meant to cite to claim 1 of US Patent No. 7,427,629. If such a rejection is made, applicants can then consider whether filing a terminal disclaimer is appropriate or not.

[22] Final Office Action mailed 1/27/09 at 2.

CONCLUSION

For the foregoing reasons, appellants respectfully submit that the Examiner has erred in rejecting this application. Please reverse the Examiner on all counts.

Respectfully submitted,

July 27, 2009
Date

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CLAIMS APPENDIX

1. (Previously presented) An IRM-support complex comprising an IRM compound that is a TLR agonist selected from the group consisting of TLR6, TLR7, TLR8, and combinations thereof, and selected from the group consisting of imidazoquinoline amines; tetrahydroimidazoquinoline amines; and imidazopyridine amines; 1,2-bridged imidazoquinoline amines; 6,7-fused cycloalkylimidazopyridine amines; imidazonaphthyridine amines; tetrahydroimidazonaphthyridine amines; oxazoloquinoline amines; thiazoloquinoline amines; oxazolopyridine amines; thiazolopyridine amines; oxazolonaphthyridine amines; thiazolonaphthyridine amines; 1*H*-imidazo dimers fused to pyridine amines, quinoline amines, tetrahydroquinoline amines, naphthyridine amines, or tetrahydronaphthyridine amines; and combinations thereof; covalently bonded to a macromolecular support material.

2. (Canceled)

3. (Original) The IRM-support complex of claim 1, wherein the macromolecular support material is selected from the group consisting of a gel, a foam, a sponge, a fiber, a hydrogel, and a bead.

4. (Canceled)

5. (Canceled)

6. (Cancelled)

7. (Cancelled)

8. (Cancelled)

9. (Cancelled)

10. (Withdrawn) The IRM-support complex of claim 1, wherein the IRM compound comprises a 4-aminopyrimidine fused to a five-membered nitrogen containing heterocyclic ring.

11. (Original) The IRM-support complex of claim 1, wherein the macromolecular support material has an average largest dimension of at least 1 nm.

12. (Currently amended) An IRM-support complex comprising an immune response modifier covalently bonded to a polymer.

13. (Canceled)

14. (Original) The IRM-support complex of claim 13, wherein the polymer is a bioadhesive polymer.

15. (Withdrawn) A medical article coated with the IRM-support complex of claim 12.

16. (Withdrawn) A medical article comprising an IRM-support complex, wherein the IRM-support complex comprises an IRM compound attached to a macromolecular support material.

17. (Withdrawn) The medical article of claim 16, wherein the medical article is selected from the group consisting of a stent, a shunt, an artificial valve, a suture, a surgical clip, a surgical staple, an indwelling catheter, a dental implant, an orthopedic implant, a surgical prosthetic, an implantable vascular access port, an artificial heart, a ventricular assist pump, a blood oxygenator, a blood filter, a hemodialysis unit, a hemoperfusion unit, a conduit tube within a heart lung machine, a tube within a dialysis apparatus, a tube within a plasmapheresis unit, an artificial pancreas, an artificial liver, an artificial lung, an intraocular lens, and a contact lens.

18. (Withdrawn) The medical article of claim 17 which is an implantable device.

19. (Withdrawn) A stent, shunt, or valve comprising a surface having an immune response modifier attached thereto.

20. (Withdrawn) The stent, shunt, or valve of claim 19, wherein the immune response modifier is covalently attached to the surface of the stent, shunt, or valve.

21. (Withdrawn) A medical article having disposed thereon an IRM, with the proviso that the medical article is not a periochip.

22. (Withdrawn) The medical article of claim 21 selected from the group consisting of a stent, a shunt, an artificial valve, a suture, a surgical clip, a surgical staple, an indwelling catheter, a dental implant, an orthopedic implant, a surgical prosthetic, an implantable vascular access port, an artificial heart, a ventricular assist pump, a blood oxygenator, a blood filter, a hemodialysis unit, a hemoperfusion unit, a conduit tube within a heart lung machine, a tube within a dialysis apparatus, a tube within a plasmapheresis unit, an artificial pancreas, an artificial liver, an artificial lung, an intraocular lens, and a contact lens.

23. (Withdrawn) The medical article of claim 22 which is a stent.

24. (Withdrawn) A formulation comprising an IRM-support complex comprising a first immune response modifier that is attached to a macromolecular support.

25. (Withdrawn) The formulation of claim 24 further comprising a second immune response modifier that is not attached to the macromolecular support material.

26. (Withdrawn) The formulation of claim 24 further comprising a solvent.

27. (Withdrawn) The formulation of claim 24 which is in the form of a gel.

28. (Withdrawn) A method of making an IRM-support complex comprising attaching an immune response modifier to a macromolecular support material.

29. (Withdrawn) The method of claim 28, wherein the immune response modifier is covalently attached to the macromolecular support material.

30. (Withdrawn) The method of claim 28, wherein the method comprises modifying the IRM to comprise an alkoxysilane moiety.

31. (Withdrawn) The method of claim 30, wherein the IRM-modified alkoxysilane is attached to a silicon-containing support material.

32. (Withdrawn) A method of treating a viral infection in a subject comprising administering to the subject an IRM-support complex of claim 1.

33. (Withdrawn) The method of claim 32, wherein the IRM-support complex is administered orally, nasally, ocularly, vaginally, transcutaneously, or rectally.

34. (Withdrawn) A method of treating an atopic immune response in a subject comprising administering to the subject an IRM-support complex of claim 1.

35. (Withdrawn) The method of claim 34, wherein the IRM-substrate is administered orally, nasally, vaginally, ocularly, transcutaneously, or rectally.

36. (Withdrawn) A method of preventing the restenosis in a subject comprising implanting into the subject a stent having an IRM attached thereto.

37. (Withdrawn) A method of preventing the restenosis in a subject comprising implanting into the subject a stent having an IRM disposed thereon.

38. (Withdrawn) The method of claim 37, wherein the IRM compound is an agonist of at least one TLR.

39. (Withdrawn) The method of claim 38, wherein the TLR is selected from the group consisting of TLR6, TLR7, TLR8, and combinations thereof.

40. (Withdrawn) The method of claim 37, wherein the IRM compound is a small molecule immune response modifier.

41. (Withdrawn) The method of claim 37, wherein the IRM compound is selected from the group consisting of imidazoquinoline amines; tetrahydroimidazoquinoline amines; and imidazopyridine amines; 1,2-bridged imidazoquinoline amines; 6,7-fused cycloalkylimidazopyridine amines; imidazonaphthyridine amines; tetrahydroimidazonaphthyridine amines; oxazoloquinoline amines; thiazoloquinoline amines; oxazolopyridine amines; thiazolopyridine amines; oxazolonaphthyridine amines; thiazolonaphthyridine amines; 1*H*-imidazo dimers fused to pyridine amines, quinoline amines, tetrahydroquinoline amines, naphthyridine amines, or tetrahydronaphthyridine amines; and combinations thereof.

42. (Withdrawn) The method of claim 37, wherein the IRM compound is selected from the group consisting of purines, imidazoquinoline amides, benzimidazoles, 1*H*-imidazopyridines, adenines, and derivatives thereof.

43. (Withdrawn) The method of claim 37, wherein the IRM compound comprises a 2-aminopyridine fused to a five-membered nitrogen-containing heterocyclic ring.

44. (Withdrawn) The method of claim 37, wherein the IRM compound comprises a 4-aminopyrimidine fused to a five-membered nitrogen containing heterocyclic ring.

45. (Withdrawn) A method of modifying the cytokine induction profile of an IRM by attaching the IRM to a macromolecular support complex.

46. (Withdrawn) The method of claim 45, wherein the cytokine induction profile is modified in favor of interferon α induction.

47. (Withdrawn) A method of preventing systemic adsorption of an immune response modifier by a subject comprising administering to the subject an IRM-support complex comprising said immune response modifier attached to a macromolecular support material.

48. (Withdrawn) A method of activating dendritic cells by permitting the cells contact an IRM compound attached to a macromolecular support material.

49. (Withdrawn) A method of treating solid tumors in a subject comprising administering to the subject an IRM-support complex comprising an IRM compound attached to a macromolecular support material.

50. (Withdrawn) A method of treating cervical dysplasia in a subject comprising applying to the cervix an IRM-support complex comprising an IRM compound attached to a macromolecular support material.

51. (Withdrawn) A method of treating bladder cancer in a subject comprising applying to the bladder an IRM support complex comprising an IRM compound attached to a macromolecular support material.

EVIDENCE APPENDIX

None.

RELATED PROCEEDINGS APPENDIX

None.